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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,444	03/20/2001	Brent Iverson	MXGN:005USC2	3269

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,444	IVERSON ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *38-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/03/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I, claims 1-37, in the reply filed on December 13, 2004 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 lacks a corresponding step. The preamble recites a method of selecting a polypeptide but lacks a step of selecting a polypeptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 11, 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Slamon et al. (US 4,918,162).

Slamon teaches methods for identifying and monitoring human cancers. The methods rely on the detection of N-myc protein in a biological specimen, usually a cell sample such as tissue sample or sputum sample. Presence of the N-myc protein in the

biological specimen may be diagnostic and/or prognostic of the cancer. Polypeptides and antibodies are used for detecting the N-myc proteins, where the polypeptides are associated with immunogenic sites on the protein. The polypeptides may be natural or synthetic. Such polypeptides include the N-myc protein in substantially pure form as well as fragments thereof. Monoclonal or polyclonal antibodies against the polypeptides are prepared by conventional techniques. Six polypeptides capable of eliciting antibodies useful in the present method have been identified. The method of synthesizing the polypeptides involves the expression in cultured cells of recombinant DNA molecules encoding a desired portion of the N-myc gene. Suitable cDNA and genomic libraries may be obtained from human cell lines known to contain the N-myc gene. (see col. 1, line 65-col. 2, line 48; col. 4, lines 36-49). The natural or synthetic DNA fragments coding for a desired N-myc fragment will be incorporated in DNA constructs capable of introduction to and expression in an in vitro cell culture. Usually, the DNA constructs will be suitable for replication in a unicellular host, such as yeast or bacteria i.e. negative bacteria E.coli. but may also be intended for introduction and integration within the genome of cultured mammalian or other eukaryotic cell lines. DNA constructs prepared for introduction into bacteria or yeast will include a replication system recognized by the host. Available expression vectors, which include the replication system and transcriptional and translational regulatory sequences together with an insertion site for the N-myc DNA sequence may be employed. (see col. 4,lines 62-68; col. 5, lines 1-15; col. 9, lines 65-66). The polypeptide can be an antibody or antibody fragment. The step of selecting a host cell that expresses the desired

polypeptides comprises the steps of contacting said antibody or antibody-fragment-expressing cells with a selected antigen; and identifying a host cell that binds to said selected antigen (see col. 9, line 23-col. 10, line 14). The vector library is obtained by administering to an animal such as a mouse a desired antigen. The mouse is then killed, the spleen removed, and the spleen cells immortalized. DNA segments that encode distinct antibodies or antibody fragments were obtained and incorporated into a plurality of expression vectors, the vectors expressing antibodies or antibody fragments on the outer membrane surface of a Gram negative host cell, E. coli. (see col. 4, lines 62-68; col. 5, line 1-68). Selected cells that express a desired antibody are subjected to cleavage to release the selected antibody or antibody fragment from the surface of the outer membrane. (see col. 7, lines 27-50).

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Georgiou et al. (US 5,348,867).

Georgiou teaches a method for selecting polypeptide from a plurality of candidate proteins comprising the steps of obtaining recombinant vectors that express fusion polypeptides at the outer membrane cell surface of a gram-negative host cell. These recombinant vectors include a functional promoter sequence and a targeting DNA sequence encoding a protein capable of targeting the outer surface of a gram-negative bacterial host cell, E. coli. The vector includes a DNA sequence, which encodes a

desired protein; expressing each of the polypeptides on the surface of a host cell; and selecting a host cell that expresses a desired polypeptide. The polypeptides are antibodies or antibody fragments. The host cell that expresses a desired antibody comprises the steps of contacting said antibody or antibody-fragment-expressing cells with a selected antigen and identifying the host cell that binds to said selected antigen (see col. 4, line 38-col. 7, line 35).

Claims 1-8, 11-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Georgiou et al. (US 5,866,344).

Georgiou '344 teaches a method of selecting a polypeptide from a plurality of candidate proteins comprising the steps of : obtaining a library of vectors that encode a plurality of distinct candidate polypeptides; wherein the vector provides for the cell surface expression of said candidate polypeptides; expressing each of said plurality of candidate polypeptides on the surface of a host cell; and selecting a host cell that expresses a desired polypeptides. (see col. 3, line 65-col. 4, line 40). Expression libraries are prepared such that an expressed protein is displayed on the surface of the cell. Typically the polypeptides will be surface expressed in a host cell such as bacterial, yeast, insect, eukaryotic or mammalian cells. Gram negative bacterial cells are preferred, particularly E. coli. Surface expression of a polypeptide, e.g. antibody, on a cell surface is achieved using a recombinant vector that promotes display on the outer membrane of a host cell. Vectors appropriate for a bacterial host cell include at least three DNA segments as part of a chimeric gene. Screening for antibodies allows one to select an antibody or antibody fragment from a plurality of candidate antibodies that

have been expressed on the surface of a host cell. The antibodies are obtained from an expressing vector library that may be prepared from DNAs encoding antibodies or antibody fragments. One source of such DNAs could be from an animal immunized with a selected antigen; or antibody genes from other sources such as those produced by hybridomas or produced by mutagenesis of a known antibody gene. One preferred method of obtaining DNA segments is to isolate mRNA from antibody cells of an immunized animal. The mRNA may be amplified and used to prepare DNA segments to include in the vectors. One may also employ DNA segments that have mutagenized from one or more DNAs that encode a selected antibody or antibody fragment. Once an antibody expression library is prepared, the selected antigen for which one desires to identify and isolate specific antibody or antibodies is labeled with a detectable label. These labels are fluorescent, chemiluminescent, etc.. The labeled antigen is contacted with the cells displaying the antibody expression library under conditions to allow specific antigen-antibody binding. Identifying antibody or antibody fragment expressing cells may be accomplished by methods that depend on the detecting the presence of the bound detectable label. A preferred method is cell sorting or flow cytometry. (see col. 3, line 65-col. 6, line 4; col. 12, lines 31-39). The selected cells that express a desired antibody are subjected to cleavage to release the selected antibody or antibody fragment from the surface of the outer membrane by adding a protease. (See example 3). The cells that bind to the selected antigen are identified by contacting said plurality of cells with detectably labeled antigen under conditions effective to allow antibody-antigen binding; removing non-specifically bound antigen from cells; and identifying the

antibody- or antibody fragment-expressing cells by detecting the presence of the label. (See col. 12, lines 14-21). The E.coli surface displayed antibodies may be rapidly and efficiently sorted using fluorescent activated cell sorting techniques (FACS) (see col. 11, lines 45-50). The cells are subjected to a first and a second round of automated cell sorting and regrowth of sorted cells is conducted between the two rounds of cell sorting. (see col. 25, lines 49-56).

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-10, 13, 14, 16-18, 25, 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Higuchi et al. (US 6,214,613).

Higuchi teaches an expression vector for preparing a library of an antibody variable region, which can express comprising polypeptides in the membrane bound form on the surfaces of eukaryotic cells. The method comprises preparing a vector, which expresses antibodies on cell membranes, concentrating the cells, which express the antibodies binding to antigen in use of marker of antigen-binding activity. Eukaryotic cells comprise being expressed polypeptides in the membrane-bound form on the

surface of the cells by introducing the vectors containing the vector to the host cells. Selecting the nucleotide sequences coding for the antibody binding to specific antigen comprising isolating the cells bound to said antigen from the group of eukaryotic cells and recovering the expression vector from the isolated cells to obtain nucleotide sequence coding for antibody variable regions bound to antigen. The method of selecting a host cell comprises immobilizing the antigen on the surface of a solid, such as magnetic particles, and isolating the cells by adhering the cells, which express the antigen-binding polypeptide, to the immobilized antigen; labeling the antigen with fluorescent substance, or magnetic beads and isolating the cells which express the antigen-binding polypeptides by flow cytometry or immunomagnetic beads method. The method for obtaining nucleotide sequence of variable region of antigen-specific antibody comprises expressing antibodies on the host cells membrane, and selecting and isolating the host cells, which express antigen-specific antibodies by means of antigen-binding activity of the antibodies, which are expressed on the membrane. (see col.3, line 5-col. 5, line 34). The host cell is E. coli.

Allowable Subject Matter

Claims 24, 27-37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior arts also fail to teach cells are subjected to a third and fourth round of automated cell sorting; said polypeptide is an enzyme and cells selecting is based on enzyme activity, which is substrate cleavage, substrate binding; wherein the cleavage of

said substrate results in a loss of quenching of a detectable signal; wherein said binding results in generation of a unique signal not found in the absence of binding; said enzyme activity results in the association of a detectable signal with said host cell; sorting said host cell by flow cytometry; and cells are subjected to a second round of automated cell sorting and a regrowth of sorted cells is conducted between the 1st and 2nd rounds.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pen see T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do

Patent Examiner
February 28, 2005

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
3/5/05